UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,744	06/02/2006	Josephus Carolus Holthuis	03-702-A	5010

20306 7590 11/24/2009

MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
11/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,744	HOLTHUIS ET AL.	
	Examiner	Art Unit	
	IQBAL H. CHOWDHURY	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/10/2008,7/29/2009* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-63* is/are pending in the application.

4a) Of the above claim(s) *1-37,44,45,47-55 and 59-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-43,46 and 56-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 January 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/16/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 of PCT/NL04/00488. .

Claims 1-63 are currently pending.

The preliminary amendment filed on 1/6/2006, amending claims 1, 3-5, 8-11, 38, 42, 44, 46-47, 50, 54, 56, 58-59 and 62-63 is acknowledged.

Election/Restriction

Applicant's election with traverse of Group XIX claim(s) 38-46 and 56-58 (in part), drawn to a method for determining whether a compound is capable of modulating an enzymatic activity displayed by a cell, wherein said enzyme is SMS and human SMS of SEQ ID NO: 12 in the communication filed on 12/10/2008 and 7/29/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-37, 44-45, 47-55 and 59-63 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions.

Claims 38-43, 46 and 56-58 are under consideration.

Priority

Acknowledgement is made of applicants claim for domestic priority under 35 USC 119(e) to US Provisional application 60/485202 filed on 7/7/2003 and claim for foreign priority under 35 U.S.C. 119(a)-(d) to a foreign patent application EPO

030789325 filed on 12/18/2003.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 1/16/2007 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is considered by the examiner. The signed copy of 1449 is enclosed herewith.

Drawings

Drawings submitted on 1/6/2006 are objected by the Examiner for the recitation of the protein sequences (Fig. 8A and 8B) without appropriate sequence identifiers i.e. SEQ ID NOs. Examiner urges the applicants to provide sequence identifiers in response to this Office action. See particularly 37 CFR 1.821(d).

Non-compliance of Sequence Rule

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that Claim 1, Fig. 8 and page 11-12, 15, 41, 46 of the specification recites the nucleic acid sequence and amino acid sequence without a corresponding sequence identifier recited. In addition, drawings (Fig. 8) submitted on 1/6/2006 are objected to by the Examiner for the recitation of the protein sequences without appropriate sequence identifiers i.e. SEQ ID NOs. See particularly 37 CFR 1.821(d).

Claim Objections

Claim 38 is objected to because of the following informalities: claim 38 is objected to as encompassing non-elected subject matter. Appropriate correction is requested.

Claim 38 is objected to because of the following informalities: claim 38 is objected to as depending from non-elected claims. Appropriate correction is requested.

Claims 39-43, 46 and 56-58 are objected to because of the following informalities: claims 39-43, 46 and 56-58 are objected to because of the recitation "A method", which should be "The method". Appropriate correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 38, which depends on claims 1-4 and 9-11 (and dependent claims 39-43, 46 and 56-58) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 38 (which depends on claims 1-4 and 9-11), wherein claim 1 recites "(a) P-L-X-D-X(35, 75)-R-R-X(8)-[YF]-X(2)-R-X(6)-T" or "(c) H-Y-[TS]-X-D-[VI]-X(3)-[FYI]-X(6)-F-X(2)-Y-H", which is confusing because it is not clear what does the phrase X(35, 75) mean? The specification also does not define clearly the meaning of said phrase. The phrases of claim 1 (upon which claim 38 depends) are also indefinite in the recitation "[YF] or [TS] or [VI] or [FYI]', which are confusing because it

is not clear whether the recitation "[YF]" means amino acid "Y" and "F" , or amino acid "Y" or "F", or amino acid either "Y" or "F". Accordingly, claims 39-43, 46 and 56-58 are also rejected, as they depend on claim 38.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 38, which depends on claims 1-4 and 9-11 (and dependent claims 39-43, 46 and 56-58) are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for determining whether a compound is capable of modulating an enzymatic activity displayed by a cell, wherein said enzyme is human SMS1 of SEQ ID NO: 12 as depicted in figure 8, wherein said compound is RNAi, SiRNA or hairpin RNA, does not reasonably provide enablement for a method for determining whether any compound is capable of modulating an enzymatic activity displayed by a cell, wherein said SMS protein is isolated from any source or said SMS protein, which is 70% identical to SEQ ID NO: 12 comprising a motif which is 80% identical to either (a) P-L-X-D-X(35, 75)-R-R-X(8)-[YF]-X(2)-R-X(6)-T or (b) C-X-D-X(3)-S-G-H-T or (c) H-Y-[TS]-X-D-[VI]-X(3)-[FYI]-X(6)-F-X(2)-Y-H of claim 1, wherein part (a) and (c) is extremely broad due to the presence of many X, which indicates any amino acid results in no structural feature, or any polypeptide which is any functional part, derivative and /or homologue of SEQ ID NO: 12 as depicted in figure 8, wherein the compound is any compound, or any RNA molecule, which modulates SMS activity. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 38, which depends on claims 1-4 and 9-11 (and dependent claims 39-43, 46 and 56-58) is so broad as to encompass a method for determining whether any compound is capable of modulating an enzymatic activity displayed by a cell, wherein said SMS protein is isolated from any source or said SMS protein, which is 70% identical to SEQ ID NO: 12 comprising a motif which is 80% identical to either (a) P-L-X-D-X(35, 75)-R-R-X(8)-[YF]-X(2)-R-X(6)-T or (b) C-X-D-X(3)-S-G-H-T or (c) H-Y-[TS]-X-D-[VI]-X(3)-[FYI]-X(6)-F-X(2)-Y-H of claim 1, wherein part (a) and (c) is extremely broad due to the presence of many X, which indicates any amino acid results in no structural feature or any polypeptide which is any functional part, derivative and /or homologue of SEQ ID NO: 12 as depicted in figure 8, wherein the compound is any compound, or any RNA molecule, which modulates SMS activity.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to extremely large number of SMS polypeptides and compounds used in the claim method broadly encompassed by the claims. However, the disclosure is limited to a human SMS1 polypeptide of SEQ ID NO: 12.

The amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of

modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. In the instant case, the protein which is 70% identical to SEQ ID NO: 12, i.e. 30% comprises many mutants, variants and fragments as well as any functional part, derivatives and/or homologue thereof. The art clearly teaches the high level of unpredictability with regard to the effect of structural changes in a protein's activity when no guidance/knowledge as to which amino acids are required for activity has been provided. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. Whisstock et al. (2003) teach that prediction of protein function from sequence and structure is a difficult problem because homologous proteins often have different functions (see abstract). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple point mutations or substitutions. Similarly, at the time of the invention, there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity. The teachings of Whisstock et al. are further supported by the teachings of Witkowski et al. (1999), where it is shown that even small amino acid changes result in enzymatic activity changes.

The specification does not support the broad scope of the claims which encompass a method for determining whether any compound is capable of modulating an enzymatic activity displayed by a cell, wherein said SMS protein is isolated from any source or said SMS protein, which is 70% identical to SEQ ID NO: 12 comprising a motif which is 80% identical to either (a) P-L-X-D-X(35, 75)-R-R-X(8)-[YF]-X(2)-R-X(6)-T or (b) C-X-D-X(3)-S-G-H-T or (c) H-Y-[TS]-X-D-[VI]-X(3)-[FYI]-X(6)-F-X(2)-Y-H of claim 1, wherein part (a) and (c) is extremely broad due to the presence of many X, which indicates any amino acid results in no structural feature or any polypeptide which is any functional part, derivative and /or homologue of SEQ ID NO: 12 as depicted in figure 8, wherein the compound is any compound, or any RNA molecule, which modulates SMS activity because the specification does **not** establish: (A) regions of the protein structure which may be modified without affecting SMS enzyme activity; (B) the general tolerance of SMS polypeptides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any SMS amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a method for determining whether any compound is capable of modulating an enzymatic activity displayed by a cell, wherein said SMS protein is isolated from any source or said SMS protein, which is 70%

identical to SEQ ID NO: 12 comprising a motif which is 80% identical to either (a) P-L-X-D-X(35, 75)-R-R-X(8)-[YF]-X(2)-R-X(6)-T or (b) C-X-D-X(3)-S-G-H-T or (c) H-Y-[TS]-X-D-[VI]-X(3)-[FYI]-X(6)-F-X(2)-Y-H of claim 1, wherein part (a) and (c) is extremely broad due to the presence of many X, which indicates any amino acid results in no structural feature or any polypeptide which is any functional part, derivative and /or homologue of SEQ ID NO: 12 as depicted in figure 8, wherein the compound is any compound, or any RNA molecule, which modulates SMS activity. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a method having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 38-43 and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Tang et al. (WO 01/53312 A1, publication 7/26/2001, see IDS).

The instant claims are drawn to a method for determining whether any compound is capable of modulating an enzymatic activity of sphingomyelin synthase (SMS)

displayed by a cell, wherein said SMS protein is isolated from any source or said SMS protein, which is 70% identical to SEQ ID NO: 12 comprising a motif which is 80% identical to either (a) P-L-X-D-X(35, 75)-R-R-X(8)-[YF]-X(2)-R-X(6)-T or (b) C-X-D-X(3)-S-G-H-T or (c) H-Y-[TS]-X-D-[VI]-X(3)-[FYI]-X(6)-F-X(2)-Y-H of claim 1, or any polypeptide which is any functional part, derivative and /or homologue of SEQ ID NO: 12 as depicted in figure 8, wherein the compound is any compound, or any RNA molecule, which modulates SMS activity.

Tang et al. teach a method for identifying an agent, which modulates human choline-phosphotransferase activity of SEQ ID NO: 3085 (alternative name of SMS), which is 100% identical to SEQ ID NO: 12 (see sequence alignment) and 100% identical to the motif (b) as recited in claim 1 of the instant application (upon which claim 38 depends), wherein the method comprises contacting the compound with the polypeptide in a cell for a time to form a polypeptide/compound complex followed by reporter gene expression such that if expression is detected, the compound binds to the polypeptide (p5, line 19-35), which modulate the polypeptide activity. Tang et al. also teach method for treatment by administering a compound that modulates the target gene products including target gene/protein expression or activity (p5, line 31-35 and p6, line 1-2). Tang et al. further teach that compound can be antisense RNA, wherein said antisense RNA will restrict mRNA expression in a particular cell or tissue (p4, line 11-18, and p20-22). Tang et al. also teach polynucleotide encoding the polypeptide of human choline-phosphotransferase activity of SEQ ID NO: 3085, vector, host cell and method of producing the polypeptide, wherein the host cell can be yeast cell, an

eukaryotic microorganism. Claim 39 is included in this rejection because fungi (yeast) and plant cell usually lack SMS and thus unable to produce sphingomyelin (SM), which is only present in animal cells (see, evidential reference Tafesse et al. 2006, Fig. 1) and thus, since, Tang et al. teach yeast host cell comprising polynucleotide encoding polypeptide, which meet the limitation of claim 39. Therefore, Tang et al. anticipate claims 38-43 and 46 of the instant application as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 56-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (WO 01/53312 A1, publication 7/26/2001, see IDS) as applied to claims 38-43 and 46 above in view of Hatch et al. (Stimulation of sphingomyelin biosynthesis by brefeldin A and sphingomyelin breakdown by okadaic acid treatment of rat hepatocytes. J Biol Chem. 1992 Jun 25;267(18):12443-51).

The instant claims are drawn to a method for determining whether any compound is capable of modulating an enzymatic activity of sphingomyelin synthase (SMS) displayed by a cell, wherein the method comprises providing said cell or fraction thereof with a labeled substrate for said SMS followed by harvesting sphingolipid and detecting labeled sphingolipid by thin layer chromatography.

Tang et al. teach a method for identifying an agent, which modulates human choline-phosphotransferase activity of SEQ ID NO: 3085 (alternative name of SMS), which is 100% identical to SEQ ID NO: 12 (see sequence alignment) and 100% identical to the motifs as recited in claim 1 of the instant application (upon which claim 38 depends), wherein the method comprises contacting the compound with the polypeptide in a cell for a time to form a polypeptide/compound complex followed by reporter gene expression such that if expression is detected, the compound binds to the polypeptide (p5, line 19-35), which modulate the polypeptide activity. Tang et al.

also teach method for treatment by administering a compound that modulates the target gene products including target gene/protein expression or activity (p5, line 31-35 and p6, line 1-2). Tang et al. further teach that compound can be antisense RNA, wherein said antisense RNA will restrict mRNA expression in a particular cell or tissue (p4, line 11-18, and p20-22). Tang et al. also teach polynucleotide encoding the polypeptide of human choline-phosphotransferase activity of SEQ ID NO: 3085, vector, host cell and method of producing the polypeptide, wherein the host cell can be yeast cell, an eukaryotic microorganism. Tang et al. do not teach use of labeled substrate for said SMS followed by harvesting sphingolipid and detecting labeled sphingolipid by thin layer chromatography.

Hatch et al. teach stimulation of sphingomyelin (SM) biosynthesis by brefeldin A in rat hepatocytes. Hatch et al. also teach use of radiolabeled [methyl-^{3}H] choline, a substrate of SM and determine the biosynthesis of radiolabeled SM in the culture media or inside the cell through thin layer chromatography (Abstract, p12444, right column, paragraph 3 and Fig. 1C), wherein brefeldin A stimulates SM biosynthesis through rapid access of the labeled phosphotidylcholine in the endoplasmic reticulum to sphingomyelin synthase (Abstract, and Fig. 4).

Hatch et al. clearly teach a method for identifying an agent, which modulates SMS activity in terms of SM biosynthesis and assay of SMS enzyme activity, which produces sphingomyelin (SM) and its modulation by a compound brefeldin A, wherein the method comprises use of labeled substrate [methyl-^{3}H] choline for said SMS followed by harvesting sphingolipid SM and detecting labeled sphingolipid SM by thin

layer chromatography.

Thus, it would have been obvious at the time of invention to one of ordinary skill in the art to combine the teachings of Tong et al. and Hatch et al. to develop a method for identifying a compound, which modulates human SMS as taught by Tong et al. and use the method of assay of SMS, which biosynthesizes sphingomyelin (SM), wherein the method comprises use of labeled substrate [methyl-^{3}H] choline for said SMS activity followed by harvesting sphingolipid SM and detecting labeled sphingolipid SM by thin layer chromatography as taught by Hatch et al. to arrive the claimed invention as claimed in claim 56-58.

One of ordinary skilled in the art would have been motivated to use radiolabeled substrate in order to monitor radiolabeled SM biosynthesis by the SMS, and thereby identify an agent or compound as stimulator or inhibitor of SMS, which can be used for treating human diseases.

One of ordinary skill in the art would have a reasonable expectation of success because Hatch et al. successfully teach a method for identifying compound which modulates sphingomyelin biosynthesis using radiolabeled substrate [methyl-^{3}H] choline, which biosynthesizes radiolabeled product SM and thereby identify compounds.

Therefore, the above references as a whole render the claims 56-58 prima facie obvious to one of ordinary skill in the art.

Conclusion

Status of the claims:

Claims 1-63 are pending.

Claims 1-37, 44-45, 47-55 and 59-63 are withdrawn.

Claims 38-43, 46 and 56-58 are rejected.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Iqbal Chowdhury, Patent Examiner
Art Unit 1652 (Recombinant Enzymes)

/Richard G Hutson/
Primary Examiner, Art Unit 1652